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(54) Title: MINIMALLY IMMUNOGENIC VARIANTS OF SDR-GRAFTED HUMANIZED ANTIBODY CC49 AND THEIR USE

(57) Abstract: Humanized anti-TAG-72 CC49 monoclonal antibodies are disclosed herein. The antibodies include a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2, and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)l, a H-CDR2, and a H-CDR3 from humanized antibody HuCC49V10. The L-CDR1, L-CDR2, L-CDR3 are within a HuCC49V10 light chain framework region that includes the corresponding amino acid from LEN at position 5, 19, 21, and 106 in the light chain. The H-CDR1, H-CDR2, and H-CDR3 are within a heavy chain HuCC49V10 framework comprising a human 21/28' CL residue at positions 20, 38, 48, 66, 67, 69, and 80 in the heavy chain. These humanized CC49 antibodies retain binding affinity for TAG-72 and have reduced immunogenicity, as compared to a parental HuCC49V10 antibody. Methods are disclosed herein for using these antibodies in the treatment or diagnosis of a tumor, such as a carcinoma, expressing TAG-72.